Information Decomposition of Short-Term Cardiovascular and Cardiorespiratory Variability

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Abstract

We present an entropy decomposition strategy aimed at quantifying how the predictive information (PI) about heart rate (HR) variability is dynamically stored in HR and is transferred to HR from arterial pressure (AP) and respiration (RS) variability according to synergistic or redundant cooperation. The PI is expressed as the sum of the self entropy (SE) of HR plus the transfer entropy (TE) from {RS,AP} to HR, quantifying respectively the information stored in the cardiac system and transferred to the cardiac system to the vascular and respiratory systems. The information transfer is further decomposed as the sum of the (unconditioned) TE from RS to HR plus the TE from SP to HR conditioned to RS. Moreover a redundancy/synergy measure is defined as the difference between unconditioned and conditioned TE from RS to HR. We show that, under the linear Gaussian assumption for the underlying multiple processes, all the proposed information dynamical measures can be calculated analytically, and present a method for their computation from the parameters of a vector autoregressive model. The method is then evaluated on a simulated process reproducing realistic HR, AP and RS rhythms, showing how known cardiovascular and cardiorespiratory mechanisms can be characterized in terms of the proposed information decomposition measures.

1. Introduction

The short-term heart rate (HR) variability is the result of the complex interplay of several regulatory mechanisms, including cardiorespiratory and cardiovascular modulations which involve respiratory (RS) and arterial pressure (AP) variability, as well as the activity of central neural commands which directly affect the cardiac system [1]. In recent years, several time series analysis methods have been proposed to link HR variability and its coupling with AP and RS variability to specific physiological mechanisms such as the cardiac baroreflex and the respiratory sinus arrhythmia [2,3]. Nevertheless, the proposed methods have been focused on single specific aspects of cardiovascular regulation (e.g., how complex is HR variability, or how it is coupled with AP or RS variability), without considering whether and how these aspects are related with each other.

On the other hand, recent developments in the field of information theory have made it possible to assess in a unified way different types of statistical dependencies inside networks of connected dynamical systems [4]. In particular, within the framework of *information dynamics* dynamical properties like complexity, causality and synergy can be expressed quantitatively exploiting a variety of entropy-based measures [4-7]. In this context, the present study introduces a decomposition strategy to represent the predictive information about the cardiac system, measured in terms of HR variability, as a sum of contributions reflecting the information dynamically stored in the system and that transferred to the system from the circulatory and respiratory systems. The strategy allows to quantify the information transfer through the baroreflex (AP→HR) and cardiopulmonary (RS→HR and RS→AP→HR) physiological pathways, as well as to infer the informational character (synergistic or redundant) of the transfer from {RS,AP} to HR variability.

After formulating information decompositions based on specific entropy-based measures, we present an approach for the exact computation of these measures in the context of vector autoregressive (VAR) modeling. The approach is then tested on realistic simulated processes reproducing typical cardiovascular and cardiorespiratory dynamics and dynamical interaction.

2. Methods

2.1. Information decomposition

In this study the respiratory, cardiac and vascular physiological systems are considered as dynamical systems, denoted respectively as X, Y and Z. The states visited by the systems over time are described as stationary stochastic processes; specifically the stochastic variables X_n, Y_n and Z_n represent respectively the RS, HR and AP variabil-

ity evaluated at the time n . Assuming Y as target system, the uncertainty about Y_n is measured by the Shannon entropy $H(y_n)$=-$\Sigma p(y_n)\cdot\log p(y_n)$, where $p(y_n)$ is the probability for the system Y to visit the state y_n at the time n. Then, considering the past system states collected in the vector variables $\boldsymbol{X}_n^-$=[X_{n-1} $X_{n-2}\cdots$], $\boldsymbol{Y}_n^-$=[Y_{n-1} $Y_{n-2}\cdots$], $\boldsymbol{Z}_n^-$=[Z_{n-1} $Z_{n-2},\cdots$], different measures of information dynamics can be computed. First, the *predictive information* (PI) of Y quantifies the resolution of uncertainty about Y_n obtained knowing the past states of all systems [4]: $P_Y=H(Y_n)-H(Y_n|\boldsymbol{X}_n^-,\boldsymbol{Y}_n^-,\boldsymbol{Z}_n^-)$.

The PI can be decomposed as $P_Y=S_Y+T_{XZ\to Y}$, where the self entropy (SE) $S_Y=H(Y_n)-H(Y_n|\boldsymbol{Y}_n^-)$ and the transfer entropy (TE) $T_{XZ\to Y}=H(Y_n|\boldsymbol{Y}_n^-)-H(Y_n|\boldsymbol{X}_n^-,\boldsymbol{Y}_n^-,\boldsymbol{Z}_n^-)$ quantify respectively the *information storage* [5] in the target system and the *information transfer* [6] from the remaining systems. The information transfer can be further decomposed as the sum of the (unconditioned) TE from X to Y and the partial (conditioned) TE from Z to Y given X, i.e., $T_{XZ\to Y}=T_{X\to Y}+T_{Z\to Y|Z}$, with $T_{X\to Y}=H(Y_n|\boldsymbol{Y}_n^-)-H(Y_n|\boldsymbol{X}_n^-,\boldsymbol{Y}_n^-)$ and $T_{Z\to Y|X}=H(Y_n|\boldsymbol{X}_n^-,\boldsymbol{Y}_n^-)-H(Y_n|\boldsymbol{X}_n^-,\boldsymbol{Y}_n^-,\boldsymbol{Z}_n^-)$. In all derivations, $H(Y_n|V)=H(Y_n,V)-H(V)$ is the entropy of the scalar variable Y_n conditioned to the vector variable V. Note that the information transfer can be alternatively decomposed as $T_{XZ\to Y}=T_{Z\to Y}+T_{X\to Y|Z}$.

Moreover, the *informational character* [7] of the driving systems X and Z in describing the target system Y is quantified in the information domain by decomposing the TE from X to Y as $T_{X\to Y}=T_{X\to Y|Z}+R_{XZ}$, where R_{XZ} is the redundant entropy (RE) of X and Z used to describe Y (note that $T_{Z\to Y}=T_{Z\to Y|X}+R_{XZ}$ holds equivalently). Expressing the RE as $R_{XZ}=T_{X\to Y}+T_{Z\to Y}-T_{XZ\to Y}$ it is easy to deduct that, if the joint system $\{X,Z\}$ contributes to the target system Y with more information than the sum of the individual contributions of X and Z, then $R_{XZ}<0$ and the driving systems act in a *synergistic* way; if, on the contrary, the separate contribution of X and Z to the information carried by Y is larger than their joint contribution, $R_{XZ}>0$ and the driving systems act in a *redundant* way.

2.2. Computation of information dynamics measures

Let us suppose that the overall process $\mathbf{U}=\{X,Y,Z\}$ has a joint Gaussian distribution. Under this assumption, the vector variable $\boldsymbol{U}_n=[X_n\,Y_n\,Z_n]^{\mathrm{T}}$ is fully described by the p^{th} order linear vector autoregressive (VAR) model [8]:

$$\boldsymbol{U}_n=\sum_{k=1}^{p}\mathbf{A}_k\,\boldsymbol{U}_{n-k}+\boldsymbol{\varepsilon}_n\,, \tag{1}$$

where $\mathbf{A}_k$ are 3×3 coefficient matrices and $\boldsymbol{\varepsilon}_n$ is a 3×1 white noise process with diagonal covariance matrix $\boldsymbol{\Lambda}$. The autocovariance of the process (1) is a sequence of 3×3 matrices $\boldsymbol{\Gamma}_k$ which are related to the VAR parameters via the Yule-Walker equations [8]:

$$\boldsymbol{\Gamma}_k=\mathrm{E}\left[\boldsymbol{U}_n\boldsymbol{U}_{n-k}^{\mathrm{T}}\right]=\sum_{l=1}^{p}\mathbf{A}_l\,\boldsymbol{\Gamma}_{k-l}+\delta_{k0}\boldsymbol{\Lambda}\,, \tag{2}$$

where δ_{k0} is the Kronecher product. To compute $\boldsymbol{\Gamma}_k$ for $k<p$, we note that (1) can be expressed as $\boldsymbol{U}_n^p=\mathbf{A}^p\boldsymbol{U}_{n-1}^p+\boldsymbol{\varepsilon}_n^p$, with $\boldsymbol{U}_n^p=[\boldsymbol{U}_n^{\mathrm{T}}\cdots\,\boldsymbol{U}_{n-p+1}^{\mathrm{T}}]^{\mathrm{T}}$, $\boldsymbol{\varepsilon}_n^p=[\boldsymbol{\varepsilon}_n^{\mathrm{T}}\cdots\mathbf{0}_{1\times p}]^{\mathrm{T}}$,

$$\mathbf{A}^p=\begin{bmatrix}\mathbf{A}_1 & \Lambda & \mathbf{A}_{p-1} & \mathbf{A}_p\\ \mathbf{I}_{3\times3} & \Lambda & \mathbf{0}_{3\times3} & \mathbf{0}_{3\times3}\\ \mathrm{M} & \mathrm{O} & \mathrm{M} & \mathrm{M}\\ \mathbf{0}_{3\times3} & \Lambda & \mathbf{I}_{3\times3} & \mathbf{0}_{3\times3}\end{bmatrix}, \tag{3}$$

and where $\boldsymbol{\Lambda}^p=\mathrm{E}[\boldsymbol{\varepsilon}_n^p\boldsymbol{\varepsilon}_n^{p\mathrm{T}}]$ is a $3p\times3p$ matrix with $\boldsymbol{\Lambda}$ as upper-left block and 0 elsewhere. Then, we find that the $3p\times3p$ covariance matrix of U_n^p is of the form

$$\boldsymbol{\Gamma}_0^p=\mathrm{E}\left[\boldsymbol{U}_n^p\boldsymbol{U}_n^{p\mathrm{T}}\right]=\begin{bmatrix}\boldsymbol{\Gamma}_0 & \boldsymbol{\Gamma}_1 & \Lambda & \boldsymbol{\Gamma}_{p-1}\\ \boldsymbol{\Gamma}_1^{\mathrm{T}} & \boldsymbol{\Gamma}_0 & \Lambda & \boldsymbol{\Gamma}_{p-2}\\ \mathrm{M} & \mathrm{M} & \mathrm{O} & \mathrm{M}\\ \boldsymbol{\Gamma}_{p-1}^{\mathrm{T}} & \boldsymbol{\Gamma}_{p-2}^{\mathrm{T}} & \Lambda & \boldsymbol{\Gamma}_0\end{bmatrix}, \tag{4}$$

and can be derived solving the discrete-time Lyapunov equation $\boldsymbol{\Gamma}_0^p=\mathbf{A}^p\boldsymbol{\Gamma}_0^p\mathbf{A}^{p\mathrm{T}}+\boldsymbol{\Lambda}^p$, thus yielding the values of $\boldsymbol{\Gamma}_0,\ldots,\boldsymbol{\Gamma}_{p-1}$. Further, from (2) we note that $\boldsymbol{\Gamma}_k$ can be calculated recursively for any $k\geq p$. exploiting the known values of $\boldsymbol{\Gamma}_{k-1},\ldots,\boldsymbol{\Gamma}_{k-p}$. With this we have shown how to compute the autocovariance sequence of a VAR process, up to arbitrarily high lags, starting from the VAR parameters $(\mathbf{A}_1,\ldots,\mathbf{A}_p,\boldsymbol{\Lambda})$. In the following we show how the elements of $\boldsymbol{\Gamma}_k$ can be exploited to calculate the information dynamics measures defined in Sect. 2.1.

Under the linear Gaussian assumption, the entropy of the target variable Y_n, and its entropy conditioned to a vector variable $\boldsymbol{V}$, can be formulated as [9]:

$$H(Y_n)=\frac{1}{2}\ln\sigma(Y_n)+\frac{1}{2}\ln(2\pi e) \tag{5}$$

$$H(Y_n\,|\,\boldsymbol{V})=\frac{1}{2}\ln\sigma(Y_n\,|\,\boldsymbol{V})+\frac{1}{2}\ln(2\pi e)\,, \tag{6}$$

where $\sigma(Y_n)$ is the variance of Y_n and $\sigma(Y_n|\boldsymbol{V})$ is the partial variance of Y_n given $\boldsymbol{V}$, which in turn can be computed as the variance of the residuals of a linear regression of Y_n on V and expressed accordingly as [9]:

$$\sigma(Y_n|\boldsymbol{V})=\sigma(Y_n)-\Sigma(Y_n,\boldsymbol{V})\,\Sigma(\boldsymbol{V})^{-1}\,\Sigma(Y_n,\boldsymbol{V})^{\mathrm{T}}, \tag{7}$$

with $\Sigma(\cdot)$ and $\Sigma(\cdot,\cdot)$ indicating respectively covariance and cross-covariance matrix. Therefore, P_Y and the terms of its decomposition (i.e, S_Y, $T_{XZ\to Y}$, $T_{X\to Y}$, $T_{X\to Y|Z}$, $T_{Z\to Y}$, $T_{Z\to Y|X}$) can all be computed from (5) and (6) letting from time to time the vector $\boldsymbol{V}$ be a proper combination of the

past system states; for practical computation, the infinite-dimensional vectors $\boldsymbol{X}_n^-$, $\boldsymbol{Y}_n^-$, $\boldsymbol{Z}_n^-$ are truncated at dimension L: $\boldsymbol{X}_n^L=[X_{n-1}\cdots X_{n-L}]$, $\boldsymbol{Y}_n^L=[Y_{n-1}\cdots Y_{n-L}]$, $\boldsymbol{Z}_n^L=[Z_{n-1}\cdots Z_{n-L}]$. Thus, the computation of information dynamics measures reduces to evaluating the covariance matrices to be combined as in (7) for getting the partial variances that, inserted in (6), allow computing any wanted conditional entropy. For instance, the covariance $\Sigma(\boldsymbol{Y}_n^L)$ is an $L\times L$ matrix containing the correlation $\Gamma_{j-i}^y=E(Y_{n-i},Y_{n-j})$ as $(i\text{-}j)^{\text{th}}$ element; the covariance $\Sigma(Y_n,\boldsymbol{Y}_n^L)$ is an $1\times L$ matrix with Γ_j^y as j^{th} element; and the covariance $\Sigma(\boldsymbol{Y}_n^L,\boldsymbol{Z}_n^L)$ is an $2L\times 2L$ matrix with $\Sigma(\boldsymbol{Y}_n^L)$, $\Sigma(\boldsymbol{Z}_n^L)$, $\Sigma(\boldsymbol{YZ}_n^L)=\{\Gamma_{j-i}^{yz}=E(Y_{n-i},Z_{n-j})\}$ and $\Sigma(\boldsymbol{YZ}_n^L)^{\mathrm{T}}$ as $L\times L$ blocks. All these matrices contain as scalar elements the covariance between lagged components of the processes X, Y, Z. As such, these matrices can be extrapolated by proper arrangement of the elements of the autocovariance sequence $\boldsymbol{\Gamma}_k$ of the overall process $\mathbf{U}$, computed as described above for k=1,...,L.

3. Validation

The proposed approach is validated on a theoretical simulation reproducing the dynamics and interactions typical of short-term cardiovascular and cardiorespiratory variability. We consider the VAR process of order p=2:

$$\begin{aligned} X_n &= 2\rho_x \cos 2\pi f_x X_{n-1} - \rho_x^2 X_{n-2} + \chi_n \\ Y_n &= 2\rho_y \cos 2\pi f_y Y_{n-1} - \rho_y^2 Y_{n-2} + C_{XY} X_{n-1} + C_{ZY} Z_{n-1} + \xi_n \\ Z_n &= 2\rho_z \cos 2\pi f_z Z_{n-1} - \rho_z^2 Z_{n-2} + C_{XZ} X_{n-2} + C_{YZ} Y_{n-2} + \nu_n \end{aligned} \quad (8)$$

where X, Y and Z are taken as descriptive of the RS, HR and AP variability, and χ_n, ξ_n, and ν_n are independent white noises with variances set to 5, 1, and 1. Each process exhibits an autonomous rhythm generated placing two complex-conjugate poles, of modulus ρ and phase $\pm 2\pi f$, in its complex plane representation. Then, interactions between processes are set by the coupling parameters C. In this study we set $\rho_z=\rho_y=0.8$, $f_z=f_y=0.1$ to reproduce oscillations at the frequency of the Mayer waves for AP and HR, and $\rho_x=0.9$, $f_x=0.3$ to reproduce narrow-band respiratory oscillations for RS [10]. Moreover, we set $C_{ZY}=0.4$, $C_{YZ}=0.1$, to reproduce the closed-loop cardiovascular coupling between AP and HR, and $C_{XZ}=0.4$, $C_{XY}=0.5$, to reproduce unidirectional vasculo-pulmonary coupling from RS to AP and cardiopulmonary coupling from RS to HR. The theoretical spectral densities of the three processes, computed from the frequency-domain representation of (8) [11], are shown in Fig. 1a.

First, we studied the dependence of the theoretical values of the information dynamics measures on the number of lags L used to compute covariance matrices. The results in Fig. 1b show that, while the PI does not vary with the lag, the SE, the TEs and the RE converge to stable

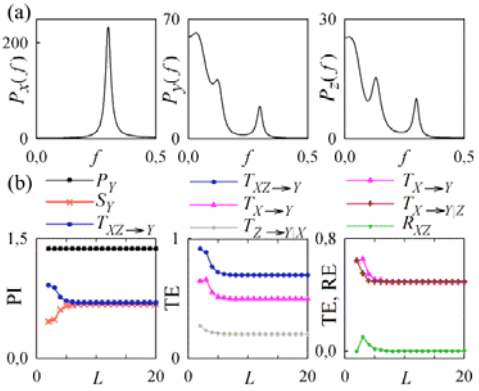

Figure 1. (a) Power spectral densities of RS (P_x), HR (P_y) and AP (P_z) simulated by (8). (b) Decompositions of the PI of HR as $P_Y=S_Y+T_{XZ\to Y}$, of the TE from {RS,AP} to HR as $T_{XZ\to Y}=T_{X\to Y}+T_{Z\to Y|X}$, and of the TE from RS to HR as $T_{X\to Y}=T_{X\to Y|Z}+R_{XZ}$, computed as a function of the length L of the past history of the observed process.

values only when L is increased. The error observed at small lags can be ascribed to an insufficient exploitation of the past history of the considered processes, which here corresponds to the truncation of the covariance sequences. It is known that the autocovariance of a VAR process decays exponentially with the lag, and that the rate of decay depends on the spectral radius of the process which in turn is related to the modulus of the largest eigenvalue of $\mathbf{A}^p$ [8]. After trying different VAR configurations, we found that all information dynamics measures get stable before ten lags, and thus we propose to use L=10 in theoretical and practical computations.

Then, we study the behavior of the various information dynamics measures at varying the simulation parameters. The results in Fig. 2 evidence for all measures a good agreement between theoretical values, computed from the actual parameters in (8), and estimated values, computed from the parameters estimated by least-squares VAR identification performed on 300-points realizations. Looking at the variations with the parameters, first we see that an increased regularity of the simulated HR variability, obtained acting on ρ_y, determines a rise of the PI exclusively due to an increased SE (all TEs were kept constant; Fig. 2a). When an enhanced baroreflex coupling is simulated by increasing C_{ZY}, we notice a stronger information transfer to the target system documented by the increase of $T_{XZ\to Y}$ and $T_{Z\to Y|X}$, but also an increase of the information storage (higher S_Y ; Fig. 2b). Interestingly, an increase of both S_Y and $T_{Z\to Y|X}$ was obtained even acting on the regularity of the driving system Z (Fig. 2c); this shows that a higher predictability of the simulated AP, obtained increasing ρ_z, enhances the PI of the simulated HR variability both in terms of information transfer and information storage. The increase of ρ_z determines also a loss of synergy between X and Z in describing Y (R_{XZ}

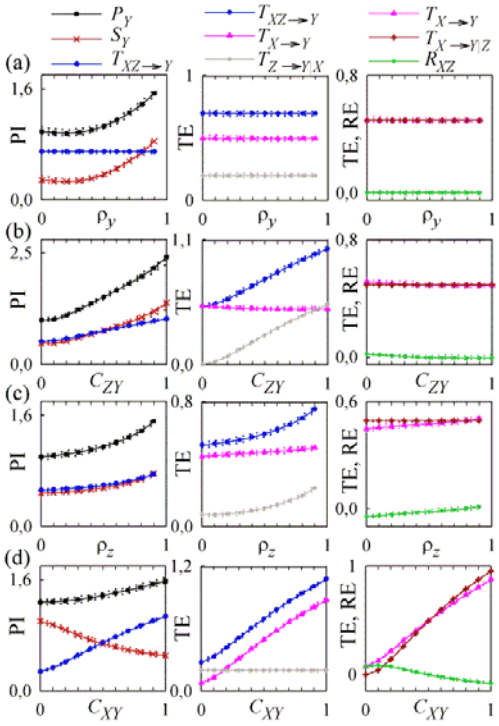

Figure 2. Information dynamics decompositions computed at varying the parameters ρ_y (a), C_{ZY} (b), ρ_z (c) and C_{XY} (d) of simulation (8). Dotted lines depict median and quantiles of each measure estimated over 100 realizations of the simulation, each of 300 points.

moves towards zero from negative values), which can be due to the fact that the information transfer $X \rightarrow Z \rightarrow Y$ becomes less detectable if Z is more regular, thus increasing the relative importance of the direct pathway $X \rightarrow Y$. A more evident transition from redundancy to synergy is noted increasing the cardiorespiratory coupling (Fig. 1d): for low values of C_{XY} simulating weak direct effects of RS on HR, the RE is positive because the information transfer from X to Y is mostly mediated by Z; for higher C_{XY} simulating stronger direct respiratory sinus arrhythmia (also documented by the increased $T_{X \rightarrow Y|Z}$), both the direct pathway $X \rightarrow Y$ and the indirect pathway $X \rightarrow Z \rightarrow Y$ were active so that the net effect was synergistic ($R_{XZ} < 0$).

4. Conclusion

The present study evidences the important role of information storage, transfer and modification in interacting with each other to give rise to the predictive information of a target dynamical system connected to multiple source systems. In fact, though confirming that different measures like SE, TE and RE reflect different aspects of information processing (respectively, regularity, causality and redundancy), our results indicate that these measured can undergo concurrent modifications in response to specific system alterations. Therefore, we advocate that the various information dynamics measures should not be computed in isolation, but rather evaluated together as components of the total statistical dependence relevant to target process of a multivariate system.

Results of the proposed realistic simulation suggest that a combined evaluation of SE, TE and RE may provide an enhanced, integrated view short-term of autonomic regulation. Future studies will be focused on exploiting these measures to assess cardiovascular and cardiorespiratory mechanisms from real HR, AP and RS time series.

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